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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/894,550	06/28/2001	Albert Collinson	BBC-083 A US	6240

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KENNETH P. ZWICKER
ABBOTT BIORESEARCH CENTER
100 RESEARCH DRIVE
WORCESTER, MA 01605

EXAMINER	
WOODWARD, CHERIE MICHELLE	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/894,550	COLLINSON ET AL.	
	Examiner	Art Unit	
	Cherie M. Woodward	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-8,11-30,32-88 and 96-104* is/are pending in the application.

4a) Of the above claim(s) *5-8,11 and 23-88* is/are withdrawn from consideration.

5)☒ Claim(s) *4 and 12-30* is/are allowed.

6)☒ Claim(s) *96-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicant's Response, filed 15 February 2007, is acknowledged. Claims 4-8, 11-30, 32-88, and 96-104 are pending. Claims 5-8, 11, and 32-88 are withdrawn as being drawn to non-elected inventions. Claims 4 and 12-30 have previously been indicated as allowable. Claims 96-104 stand rejected.

Response to Arguments

2. The rejection of claim 31 is withdrawn as moot in light of Applicant's cancellation of the claim.

Claim Rejections Maintained - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. The rejection of claims 96-104 under 35 USC 103(a) as being unpatentable over Luger, *et al* (of record) in view of Schmidt, *et al* (EP0218531) and Berg (US Patent 5622701), is maintained for the reasons of record and the reasons set forth herein.

Applicant argues that the Examiner has not set forth a *prima facie* case of obviousness by a strict construction and application of the teaching, suggestion, or motivation (TSM) test. Further, Applicant argues that there is no reason to believe that antibodies to the peptide disclosed by Schmidt et al., will bind the antigen of SEQ ID NO: 3, as disclosed by Applicant. Applicant also argues that the Examiner has engaged in hindsight reasoning in constructing the obviousness rejection. Further, Applicant argues that the Office Action of 2 August 2004, rejects dual-specific

antibodies as non-enabled. Applicant's arguments filed 15 February 2007 have been fully considered but they are not persuasive.

With regard to the strict construction and application of the TSM test, Applicant is directed to KSR v. Teleflex, Inc., No. 04-1350 (U.S. Apr. 30, 2007), which states, "rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. As our precedents make clear, however, the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." (KSR, slip op. at 14). The Court continued, stating that "helpful insights, however, need not become rigid and mandatory formulas; and when it is so applied, the TSM test is incompatible with our precedents. The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents." KSR, slip op. at 15. As such, the rejection at issue and its analysis under 103(a) meets all of the *prima facie* requirements under Graham v. Deere (1966) (*supra*) and KSR v. Teleflex (2007) (*supra*).

As stated in the Office Action of 17 August 2006, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made a dual specificity antibody with enhanced sensitivity against both IL-1α and IL-1β. Such antibodies would be able to neutralize IL-1 mediated inflammation more completely than an antibody directed against either cytokine, alone.

Luger, et al., teach a dual specific antibody to IL-1 α and IL-1 β which recognizes a common epitope on the interleukin molecules and which may be used to develop more sensitive immunoassays for the detection of IL-1 activity in body fluids during the pathogenesis of inflammatory diseases. Schmidt et al., teach the sequence of a peptide derived from IL-1β (TKGGQDITDFT) with four common amino acids shared between IL-1α and IL-1β (ITDF). The ten amino acid sequence peptide of Schmidt et al., combined with the sequence overlap with the four amino acids that are potential antigenic epitopes of both IL-1α and IL-1β is sufficient to permit antibodies raised against the peptide of Schmidt et al., to be used to bind both IL-1α and IL-1β. For example, see, Harlow et al., Eds. Antibodies, A Laboratory Manual, 1988 Cold Spring Harbor Lab. p. 42, Table 4.1. Harlow et al., teach that small synthetic peptides with six amino acid residues in length will consistently elicit antibodies that bind to the original peptide (p. 76, first paragraph under "Size of the Peptide"). Harlow et al., also state that antibodies against

smaller peptides have been reported, but generally, peptides of approximately 10 residues should be used (p. 76, first paragraph under "Size of the Peptide"). As such, it is with an understanding of the well-known teachings of Harlow et al., that the Examiner made the instant rejection under 103(a). The use of synthetic peptides as immunogens has been well known in the art since 1938 (Harlow et al., p. 72, second paragraph).

One of ordinary skill in the art at the time the invention was made would have found it *prima facie* obvious to have then added the modifications of Berg in order to humanize the antibody and make it more useful for *in vivo* applications. The person of ordinary skill in the art at the time the invention was made would have been motivated to do so because an antibody with dual specificity to IL-1 α and IL-1 β would be able to neutralize IL-1 mediated inflammation, particularly T-helper cell activation (see, i.e. Harlow et al., Eds. *supra*, p. 42, Table 4.1), more completely than an antibody directed against either cytokine, alone.

The rejection is amenable to evidence. Absent evidence to the contrary, the state of the art teaches that antibodies raised according to the teachings of Luger et al., against the peptide of Schmidt et al., which can be humanized by the modifications of Berg, will in fact bind both IL-1α and IL-1β. Applicant has not introduced any evidence to the contrary. Because the Patent Office does not have the facilities to determine whether the antibodies of Luger et al., made against the peptide of Schmidt et al., and humanized by the modifications of Berg overlap with the instantly claimed dual-specificity antibodies, the burden is on the application to show a novel and unobvious difference between the claimed antibodies and that of the prior art. See In re Brown, 59 CCPA 1036, 459 F.2d. 531, 173 USPQ 685 (CCPA 1972) (holding at 1041, "[a]s a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith") and Ex parte Gray, 10 USPQ 2d 1922, 1924-25 (PTO Bd. Pat. App. & Int.).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

With regard to Applicant's argument that the Office Action of 2 August 2004, rejects dual-specific antibodies as non-enabled, Applicant's argument is misplaced. Four sets of claim

amendments have occurred since the Office Action of 2 August 2004. The scope of enablement rejection under 35 USC 112, first paragraph, in the Office Action of 2 August 2004, was directed to claims 1-4, 12-31, and 89-95, which did not specify any particular antigenic sequence, and many of the claims pending at that time have now been cancelled or significantly amended from the claims currently under examination. Moreover, the scope of enablement rejection was withdrawn in light of Applicant's claim amendments and cancellations in the Office Action of 1 February 2006. As such, Applicant's arguments are moot in light of the intervening claim amendments.

Conclusion

Claims 4 and 12-30 are allowable.

Claims 96-104 remain rejected.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cherie M. Woodward, MA, MS, JD, whose telephone number is (571) 272-3329. The examiner can normally be reached on Monday - Friday 9:00am-5:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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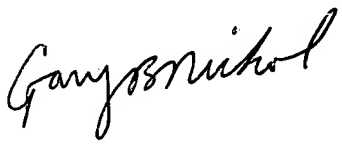

GARY B. NICKOL, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600